## REMARKS

### I. INTRODUCTION

In response to the Office Action dated August 25, 2003, claims 31, 36-39 and 44-47 have been amended. Claim 33 has been cancelled. Claims 40-43 have been withdrawn from consideration by the Examiner. Claims 31, 32, 34-39 and 44-47 remain in the application and are presently being examined. Entry of these amendments, and reconsideration of the application, as amended, is requested.

### II. CLAIM AMENDMENTS

Applicants' attorney has made amendments to the claims as indicated above. These amendments were made solely for the purpose of clarifying the language of the claims, and do not introduce new matter. Support for the amendment to claim 31 can be found in cancelled claim 33. Support for the amendment to claims 44-47 can be found in the specification at page 9, line 11, and at page 11, lines 1 and 7. Entry of these amendments is respectfully requested.

### III. INTERVIEW SUMMARY

Applicants' undersigned attorney acknowledges and appreciates the helpful comments and suggestions offered by Examiner Mosher during a telephonic interview conducted on October 7, 2003. The discussion included the definition of "synthetic peptide" and potential strategies for overcoming prior art rejections. Applicants have amended the claims and addressed outstanding issues in the arguments hereinbelow, in a manner consistent with Applicants' understanding of the Examiner's comments. Should the Examiner find that further issues remain that would interfere with allowance of the pending claims, the courtesy of a telephone call would be greatly appreciated.

### IV. RESTRICTION REQUIREMENT

At page (2) of the Office Action, newly submitted claims 40-43 were withdrawn from consideration as being directed to a non-elected invention. Because all of the claims are linked by a common inventive concept, the provision of a method of high yield synthesis of vpr that results in previously unattained synthetic vpr proteins that are stable and soluble in aqueous solution, Applicants respectfully request the Examiner reconsider and withdraw the restriction requirement.

## V. NON-ART REJECTIONS

### A. Indefiniteness

At page (2) of the Office Action, claims 33, 34, 36, 38, and 44-47 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The cancellation of claim 33 renders the rejection of this claim moot. The amendments to claim 31 clarify that "comprising" applies to all or a fragment or variant of SEQ ID NO: 1, and that sub-parts (b) and (c) refer to SEQ ID NOS: 2 and 3, respectively. The amendment of claims 44-47 to recite "product" instead of "system" removes any potential uncertainty that a composition of matter is intended, which is consistent with the recitation of physical components ("peptide" and "substrate"), rather than method steps, in the claims.

### B. Written Description

At page (3) of the Office Action, claims 34, 35, 38, 39, and 44-47 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Although Applicants pointed to portions of the specification which support these claims, these references to support in the specification are dismissed as they allegedly "do not reasonably convey the broad concept of 'bound to a second molecule comprising a DNA or protein molecule'". Applicants respectfully disagree with this assertion.

It is well known in the art (as it was at the time the present application was filed) that vpr is particularly suited for conjugation to other proteins or DNA. In addition, the specification refers to the "broad concept" in its discussion of using synthetic vpr for gene transfer (see, e.g., page 12, lines 18-22). Moreover, the usefulness of vpr molecules in fusion proteins (see, e.g., page 5, line 6) and otherwise bound to a second molecule (see, e.g., page 2, lines 27-28) is so widely known, the broad concept is readily recognized by those skilled in the art regardless of the recitation of specific examples. Even if one construes the recitation of ELISA applications as solely supporting immobilized antibody (and not the antigen bound to a second molecule), the reference to using vpr

or fragments thereof to generate antibodies (see, e.g., page 10, lines 22-23) also conveys the broad concept of vpr bound to a second molecule, as fusion proteins are often used in the art for the generation of antibodies.

The Examiner is respectfully reminded that the written description requirement does not necessitate recitation of the language *in ipsis verbis* (*In re Lukach*, 169 USPQ 795, 798, CCPA 1971). Compliance with 35 U.S.C. §112, first paragraph, "does not necessarily require specific recitations of use but may be inherent in description or may result from disclosure of a sufficient number of properties to make a use obvious; and where those of ordinary skill in the art will know how to use, the applicant has a right to rely on such knowledge". (*In re Nelson*, 126 USPQ 242, 253, CCPA 1960). Applicants maintain that one skilled in the art would readily appreciate a description of vpr peptides bound to DNA or protein molecules from the specification as filed.

**C. Enablement**

At page (4) of the Office Action, claims 36-39 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such as way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is based on an assertion that the specification does not teach any treatment method of using the claimed peptides. Applicants respectfully disagree, as the specification recites a number of therapeutic uses for the claimed peptides, e.g., at page 10, line 26, and at page 12, as well as original claims 28-30. In addition, the Examiner alleges that "a search of the prior art does not indicate routine knowledge of successful treatment methods using HIV VPR peptides." Yet the prior art cited by the Examiner discloses several treatment methods using HIV VPR peptides (see, e.g., Abstracts of Azad and Weiner). In fact, the Examiner has even stated at page 6 of the Office Action, that it would have been obvious to prepare a pharmaceutical composition containing vpr protein for therapeutic use. To facilitate prosecution, however, Applicants have amended claim 36-39 to delete "pharmaceutical".

At page (5) of the Office Action, claims 31, 34, 36, 38, 44, and 46 were rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the recited VPR fragments, does not reasonably provide enablement for variant peptides SEQ ID NO:8 and 9. The Examiner alleges that "the specification does not suggest how to use variant peptides which do not

match the sequence of VPR from any known strain of HIV". Applicants respectfully disagree with this statement.

The specification, at page 6, lines 20-21, discloses the use of the vpr peptides of the invention for epitope mapping and isoelectric focusing. At pages 27-30 of the application, namely originally-filed claims 9-30, numerous uses for vpr peptides having mutations that substitute the native prolines (as do SEQ ID NO: 8 and 9) are described. The utility of substitution for these prolines is discussed in material that can be found in the record at pages 6-8 (Example 19) of the Preliminary Amendment submitted with the application as filed on August 20, 2001. In particular, the Examiner's attention is directed to page 8, lines 1-7, of this Amendment. As discussed therein, those skilled in the art recognize that the substitution of asparagine for proline would allow for a similar effect (to proline) on the protein backbone, but without being able to undergo cis/trans isomerism, rendering them ideal for structural analyses using NMR and X-ray crystallography.

Accordingly, Applicants respectfully request the Examiner reconsider and withdraw the rejections based on 35 U.S.C. §112.

## VI. PRIOR ART REJECTIONS

At page (5) of the Office Action, claims 31, 32, and 36 were rejected under 35 U.S.C. §102(b) as being anticipated by Azad, WO 95/26361 (Azad). Also at page (5) of the Office Action, claim 31 was rejected under 35 U.S.C. §102(b) as being anticipated by Sette et al., WO 98/32456 (Sette). At page (6) of the Office Action, claims 31, 34, and 44 were rejected under 35 U.S.C. §102(b) as being anticipated by Koprowski et al., WO 98/08375 (Koprowski). At page (6) of the Office Action claims 35 and 37 were rejected under 35 U.S.C. §103(a) as being unpatentable over Azad. At page (7) of the Office Action, claims 33, 34, 37, and 38 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sette. At page (7) of the Office Action, claims 31-39 were rejected under 35 U.S.C. §103(a) as being unpatentable over Weiner et al., WO 96/08970 (Weiner).

Applicants respectfully traverse these rejections.

None of the cited references discloses a synthetic vpr protein having the amino acid sequence shown in SEQ ID NO: 1. Applicants respectfully note that "synthetic" is defined in the specification at page 9, lines 22-25, as referring to "solid phase peptide synthesis". As discussed at page 9, lines 10-14, the ability to successfully produce a synthetic vpr was surprising and unexpected

given the results of previous attempts to provide a useful vpr protein via synthetic or recombinant methods. The synthetic vpr proteins of the invention, even at mM concentrations, are very soluble in water and remain stable without any sign of protein aggregation and protein precipitation.

In contrast, the vpr proteins described in the cited references are made by yeast cells (Azad) or plant cells (Koprowski), and not via solid phase peptide synthesis. Moreover, the fragments described in the cited references are not encompassed by Applicants claims.

As discussed above, the successful synthesis of vpr without problems involving protein aggregation and solubility in aqueous solution was unexpected. Thus, the various compositions and uses recited in claims 31-39 cannot be regarded as obvious, as the problems discussed in the review of the prior art at pages 2-5 of Applicants specification would have prevented them from being enabled. The ability to prepare and use compositions comprising synthetic vpr is not taught or suggested in the Azad, Weiner, Sette, or Koprowski references cited by the Examiner. Accordingly, Applicants respectfully request the Examiner reconsider and withdraw the rejections based on the prior art.

## VII. CONCLUSION

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,



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